Remarks

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

Claims 1-3, 5-7, 9, and 10 have been amended and claim 4 has been canceled without prejudice. New claims 40-48 have been added. Claims 1-3, 5-10, and 40-48 are pending.

The rejection of claims 1 and 4-10 under 35 U.S.C. § 112 (first paragraph) for lack of enablement is rendered moot with respect to claims 1 and 4-10, and is respectfully traversed with respect to new claims 40-48.

The PTO has taken the position that the specification does not provide enablement for "nucleic acids that hybridize under conditions of unspecified stringency to SEQ ID NO: 1" (office action at page 3). Claim 40 does, however, recite both the hybridization conditions ("hybridization conditions comprising hybridization at 50°C for 24 hours in a solution that comprises 6X SSC and 0.5% SDS, followed by wash conditions comprising a first wash at 45°C in a solution that comprises 2X SSC and a second wash at 45°C in a solution that comprises 0.1X SSC") and the function of the polypeptide encoded by the claimed DNA molecule ("elicits a hypersensitive response in non-host plants"). Therefore, this basis of rejection is overcome.

The PTO also takes the position at page 3 of the outstanding office action that the present applicant must also teach, in addition to SEQ ID NO: 1, the sequence of other DNA molecules that hybridize to the complement of SEQ ID NO: 1. Applicants disagree.

To enable a person of skill in the art to practice the presently claimed subject matter, the specification need only provide objective enablement. *See In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). In other words, as long as the specification teaches those of skill in the art how to obtain and use other species encompassed by the presently claimed genus, the specification is enabling. That is certainly the case presented here.

Applicants have identified a single species of *hrpW* by its nucleotide sequence (as well as the amino acid sequence of its encoded HrpW protein) and demonstrated, via Southern hybridization, that *hrpW* is indeed widespread among *Erwinia* pathogens (*see* Example 17 at pages 30-31). Thus, to obtain other species encompassed by the present invention, one of skill in the art would need only to reproduce the results of the Southern procedure described in the present application and isolate the hybridizing DNA molecules

therefrom (i.e., the DNA from other *Erwinia* pathogens will be present in the distinct bands, labeled by the *hrpW* probe). Because the stringency conditions recited in claim 40 are sufficiently high, one of skill in the art would reasonably expect hybridizing genomic DNA to encode a polypeptide that also possesses activity as a hypersensitive response elicitor. To isolate the genomic DNA and then sequence the same would require nothing more than routine experimentation, and the PTO has not suggested otherwise. Testing of the activity, to confirm that the encoded polypeptide does in fact possess hypersensitive response elicitor activity, can be carried out as described in the present application (*see* page 11, line 3 to page 14, line 19, describing recombinant techniques and protein purification procedures; page 29, lines 12-24 and Figure 5A, describing infiltration of elicitor preparation onto tobacco leaves to assay for induction of hypersensitive response-like necrosis). Thus, one of skill in the art is fully able to obtain and use other DNA molecules that hybridize under the conditions recited in claim 40, and then use those DNA molecules to obtain their encoded polypeptides.

The PTO does not appear to contest the fact that one of skill in the art would have been fully able to make and use the presently claimed subject matter of claim 40, but instead takes the position that applicant must have both isolated and sequenced hybridizing nucleic acids. The PTO's position is unsupported by the law, which as noted above requires nothing more than objective enablement. Given that applicants have identified SEQ ID NO: 1 and demonstrated that homologous nucleic acid sequences are indeed conserved among *Erwinia* pathogen, applicants have fully satisfied the requirements of objective enablement.

As evidence that one of skill in the art would reasonably have expected hybridizing nucleic acid molecules to encode hypersensitive response elicitor polypeptides, applicants refer to the attached Exhibit 1, which contains Genbank Accession AY237642 (*hrpW* of *Erwinia pyrifolia*) and a ClustalW alignment that shows the *E. pyrifolia hrpW* sequence is highly identical (~83 percent identity) to the *E. amylovora hrpW* of SEQ ID NO: 1. Because the *E. pyrifolia hrpW* nucleotide sequence is highly conserved with the *E. amylovora hrpW* sequence of SEQ ID NO: 1, and the *E. pyrifolia hrpW* would therefore have hybridized to the complement of the *E. amylovora hrpW* sequence, this confirms the reasonableness of correlating the hybridization results with functional activity as a hypersensitive response elicitor.

For these reasons, applicants submit that the invention of claims 1 and 4-10 as well as new claims 40-48 are fully enabled by the disclosure of the present application. The rejection of claims 1 and 4-10 should be withdrawn and should not be applied to new claims 40-48.

The rejection of claims 1 and 4-10 under 35 U.S.C. § 112 (first paragraph) for lack of written descriptive support is rendered moot with respect to claims 1 and 4-10, and is respectfully traversed with respect to new claims 40-48.

For substantially the same reasons as noted above, one of ordinary skill in the art would fully recognize that applicants were in possession of isolated DNA molecules from other species of *Erwinia* that encode HrpW homologs. Applicants have identified a single species of *hrpW* by its nucleotide sequence (as well as the amino acid sequence of its encoded HrpW protein) and demonstrated, via the above-mentioned Southern hybridization procedures, that *hrpW* is indeed widespread among *Erwinia* pathogens (*see* Example 17 at pages 30-31).

In addition, the HrpW protein of SEQ ID NO: 2 is disclosed in the present application to share properties with other known hypersensitive response elicitors, including: characteristic amino acid composition such as being glycine rich and lacking in cysteine, heat-stability, low mobility in SDS-PAGE, and ability to elicit a hypersensitive response in non-host plants (*see* (page 9, lines 11-14 as previously amended; page 27, lines 19 to page 28, line 4; and page 29, lines 12-24; and page 31, line 3 to page 32, line 2). That these properties are shared by the art-recognized class of proteinaceous hypersensitive response elicitors is evident not only in the specification, but also in the prior art (*see* Bonas I, Bonas II, Preston, cited in and attached to response submitted on March 22, 2002). The structural property that distinguishes HrpW of *Erwinia* from previously identified hypersensitive response elicitor proteins, such as HrpN of *Erwinia*, HrpZ of *Pseudomonas*, and PopA of *Ralstonia*, is the presence of two distinct domains, the N-terminal hypersensitive response elicitor domain and the C-terminal pectate lyase-like domain (which, though homologous, was shown not to possess pectate lyase activity). While this same structural feature is present in HrpW of *Pseudomonas* and its homologs, the *Pseudomonas syringae* pv. *tomato* DC3000 *hrpW* probe was demonstrated not to hybridize with genomic DNA of several *Erwinia* pathogens, include *Erwinia amylovora* (*see* Charkowski et al., "The *Pseudomonas syringae* pv. tomato HrpW Protein Has Domains Similar to Harpins and Pectate Lyases and Can Elicit the Plant Hypersensitive Response and Bind to Pectate," *J. Bacteriol.* 180(19):5211-5217 (1998) at 5214 and Fig. 2 (copy attached as Exhibit 2)). Thus, the hybridization conditions recited in claim 40 would not be expected to result in hybridization with *Pseudomonas hrpW* homologs.

Given the above demonstration by applicants, one of ordinary skill in the art would have understood that applicants were in possession of not just the isolated DNA molecule of SEQ ID NO: 1, but also the other isolated DNA molecules that applicants identified in the Southern hybridization experiments (by virtue of their hybridization to the

hrpW probe). Given applicants' demonstration of hybridization to the DNA molecule of SEQ ID NO: 1 under the recited hybridization and wash conditions, one of ordinary skill in the art would have expected hyridizing DNA molecules from other *Erwinia* species to similarly encode proteins capable of inducing a hypersensitive response-like necrosis in non-host plant tissues. Therefore, written descriptive support does indeed exist for the presently claimed invention.

Despite the identification of a single species by sequence and the demonstration by Southern hybridization that homologs are indeed present among other *Erwinia* pathogen, the PTO suggests that applicants instead must have sequenced the hybridizing nucleic acids. Applicants disagree.

The burden of establishing that an application lacks adequate written descriptive support falls on the PTO. *See In re Wertheim*, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976) ("[T]he PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims."). According to the Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶1, "Written Description" Requirement, 66 Fed. Reg. 1099 (January 5, 2001) ("Written Description Guidelines"), when the genus represents widely variant species more than one species is required, yet when the genus represents closely related species as few as one species may be sufficient. 66 Fed. Reg. at 1106. Thus, size of the genus is clearly of less import than variance of species within the genus. In this case, the *direct* evidence presented in the specification demonstrates that variance is at a minimum given the recited hybridization and wash conditions. The PTO, on the other hand, has provided no evidence concerning variance within the genus.

Instead, the PTO cites to language from *Univ. of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) to support its position that one disclosed sequence cannot provide descriptive support for the presently claimed genus. This position is untenable, lacking support in the Written Description Guidelines and in the law. Firstly, the Written Description Guidelines do not unequivocally recite that one disclosed sequence cannot provide descriptive support for a genus. 66 Fed. Reg. at 1106. Secondly, *Eli Lilly* actually supports applicants' position. In *Eli Lilly*, the Federal Circuit addressed the validity of several claims of U.S. Patent No. 4,652,525 to Rutter et al. ("Rutter"), specifically those claims that recited the limitations 'vertebrate,' 'mammalian,' or 'human' cDNA for insulin. Rutter disclosed the nucleotide and amino acid sequences of a rat cDNA encoding insulin, but merely described a general procedure for obtaining the human cDNA encoding insulin. *Id.* at 1567, 43 USPQ2d at 1405. The Federal Circuit found that the description of the rat

cDNA did not provide adequate descriptive support for the narrow subgenus of 'human' cDNA (no species disclosed), the larger subgenus of 'mammalian' cDNA (only one (rat) species disclosed), and the larger genus of 'vertebrate' cDNA (only one (rat) species disclosed). *Id.* at 1567-68, 43 USPQ2d at 1405. The Federal Circuit did note, however, the district court's statement that the specification provided adequate written descriptive support for the subgenus of 'rat' cDNA encoding insulin. *Id.* at 1566.

In the present case, claims 40-48 are not just directed to *Erwinia hrpW* (akin to claims of Rutter that recited 'rat' cDNA), but more narrowly to those isolated *Erwinia* DNA sequences that both hybridize to the complement of SEQ ID NO: 1 under the recited stringency conditions and encode a polypeptide that elicits a hypersensitive response in non-host plants. These stringency conditions are the same utilized by applicant in Examples 8 and 17, and support applicants' demonstration that *hrpW* is distributed among *Erwinia* pathogen. From the foregoing, it should be appreciated that the present application provides more than simply a single nucleotide sequence of an *Erwinia hrpW* DNA molecule in isolated form. It should also be appreciated that the presently claimed genus is actually more narrowly defined, given the recited hybridization conditions and activity, than the subgenus of 'rat' cDNA that was indicated, as noted above, to be adequately described in the Rutter patent.

Based on these hybridization results presented in the specification and the hybridization conditions recited in claim 40, the presently claimed genus is clearly not at all akin to those claims held invalid in *Eli Lilly* but, instead, more alike claimed subject matter that was stated in *Eli Lilly* to have been adequately described. Knowing that one species may adequately define a genus lacking substantial variation, one of skill in the art would understand that applicants were in possession of the presently recited genus.

For these reasons, applicants submit that the invention of claims 1 and 4-10 as well as new claims 40-48 are in compliance with the written description requirement. The rejection of claims 1 and 4-10 should be withdrawn and should not be applied to new claims 40-48.

The rejection of claims 1-10 under 35 U.S.C. § 112 (second paragraph) for indefiniteness is respectfully traversed in view of the above amendments. This rejection should be withdrawn.

The various objections to claims 2-5, 7, and 9-10 have been obviated by the above amendments and should therefore be withdrawn.

In view of the all of the foregoing, applicants submit that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

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